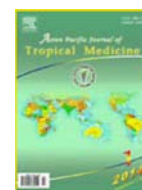




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The chemical composition, botanical characteristic and biological activities of *Borago officinalis*: a review

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ABSTRACT

Borage (*Borago officinalis*) is an annual herb which is cultivated for medicinal and culinary uses, although it is commercially cultivated for borage seed oil. Borage seed oil is the plant rich in the gamma-linolenic acid (26%–38%) which is used as dietary or food supplement. Other than seed oil it contains a lot of fatty acids such as linoleic acid (35%–38%), oleic acid (16%–20%), palmitic acid (10%–11%), stearic acid (3.5%–4.5%), eicosenoic acid (3.5%–5.5%) and erucic acid (1.5%–3.5%). It is used for the treatment of various diseases such as multiple sclerosis, diabetes, heart diseases, arthritis and eczema. In this study different aspects of borage such as plant characteristics, production, applications in traditional medicine, clinical considerations, its effects on patients' blood and urine biochemistry, and also the effect of the its products on liver and kidney performance tests are presented using published articles in scientific sites.

1. Introduction

Borago officinalis or borage is an annual herb which is cultivated for medicinal and culinary uses, even though it is commercially cultivated for borage seed oil. Borage seeds oil is the richest plant source of the gamma-linolenic acid (GLA) which is used as dietary or food supplement.

GLA is sometimes prescribed as anti-inflammatory drug with this belief that it lacks some of the common side-effects of other anti-inflammatory drugs. GLA is also used for the treatment of multiple sclerosis, diabetes, heart diseases, arthritis, eczema, autoimmune disorders, cancer and premenstrual syndrome[1,2].

Borage is a medicinal plant which has different usages

in pharmaceutical, industrial and forage fields and is used in production of drinks and salads. This plant is known as high plant in Mediterranean regions. Borage is cultivated around the world but is native to Europe, North Africa and Asia Minor[3,4]. Borage has oil seed which contains a high amount of the GLA (30%–40%). GLA is one of the volatile fatty acids which is synthesized just by a few plant varieties and often found in their seeds[5]. The main sources of the GLA are borage and evening primrose[6,7]. Borage produces 300 to 600 kg seed in Britain so as to increase the amount of GLA in available crops and produce GLA in common oilseed productions[7,8]. Ninety percent of selling rate of GLA oil is related to evening primrose. But borage is a better resource of the GLA since its seeds contain 30%–40% oil of which 20%–30% is GLA. This amount is approximately twice as many as that of in evening primrose. The oil of borage is more constant and its process is simpler than the oil of the evening primrose[7,10].

In this study different aspects of borage such as plant's history, characteristics, production, applications in traditional medicine, clinical considerations, its effects on

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patients' blood and urine biochemistry, and also effect of the its products on liver and kidney performance tests are presented.

2. History

It was supposed that main sources of borage are from Syria and Asia Minor while this plant is just found in very little amounts. It seems that this plant has originated from west Mediterranean areas, Spain and North Africa and then has naturalized in many other locations. Historical documents shows that people from North Africa tribes have transferred it to Spain and then to other regions^[11–14]. However, most researchers say that this plant is native to Mediterranean areas^[15].

2.1. Botanical characteristics

Borago officinalis from Boraginaceae family is known as borage, burrage, bourrache, and bugloss^[16–19]. Borage is an annual, herbaceous and hairy plant which height changes between 70 to 100 cm^[3,20]. Stems are straight, often branched^[21], hollow, and covered by tough fibers. Its leaves are alternate and simple. Its leaves are covered with tough fibers^[22]. The flowers are blue and rarely appear white or rose colored^[23]. Their calycle and corolla are five-parts which are divided into some parts and make flowers polypetalous appearance. One of the features of the corolla is that lamina parts lead to a tube which is almost seen in plants in this family, which differentiates it from other various plants. Each flower has five flags with anthers near to each other and there is a vertical appendage in their tube base. The pistil has a superior ovary which is changed to a fruit with 3 to 4 brownish nutlet after growing and there is a dark but no albumin seed inside each. The fruit of borage is a small brownish oval wrinkled nutlet^[24]. Ripe nutlets are dark without albumin^[23].

2.2. Ecology

It is a high plant with high resistance to cold which can grow well in wet soils with good drainage, weedy places and in complete exposure to sunlight. It cannot tolerate poor dry soils but growth condition can be better in suitable conditions. It can also grow better in land exposed to moderate sun. Intense sun can change plant to rosette state^[14,21,22,25]. This plant can grow in each type of soil and in pH scale range from 4.5–8.2. The suitable pH for this plant is 6.6. It has been reported that borage can be easily cultivated in medium or heavy soils with salt water. Regarding its high potential in taking sodium and chlorine, it is likely suitable to modify salt soils^[23,26–28].

2.3. Cultivation

This plant is reproduced through seeding and each seed weights almost 17 to 19 g. Seeds are sown at 5–7 kg each hectare. The recommended suitable density to plant borage is equal to 100 000 shrubs per hectare. In another research in Isfahan, 30 cm distance between rows and 10 cm distance between shrubs on row has been defined as the best attendance. Suitable cultivation time for this plant is in early spring, and it also can be cultivated in autumn and late winter^[21,23]. Researchers have shown that early seeding increases seed performance comparing with late seeding. There is an interaction between seed performance and GLA level which could be related to the date of cultivation and the consumption of nitrogen fertilizer^[1,29]. In early seeding grain filling was happened in warmer days of mid-June to late August. Obtained results is shown that the amount of the GLA is reduced as temperature reduction during growth period in a way that matched other studies on oil seed crops^[30].

Nitrogen fertilizer increases length of the plant, twigs and production efficiency. The most adequate amount of fertilizer is 250 kg of Nitrogen per hectare but more amounts will decrease production efficiency. Mineral fertilizers are not usually used in planting borage. In order to grow this plant properly, not only the amount of nitrogen and phosphorus but the amount of potassium in soil should be enough^[23,31]. Since flowering twigs are medicinal it is necessary to collect them and then dry and pack according to correct principles. This plant is harvested in flowering period before the start of seed formation^[5,9,32].

They should be dried in fresh air in shadow or by dryer in temperature of 40 °C. Three or four harvest is done according to climate condition. The yield of borage is between 1500–2500 kg dried plants per hectare^[5,32,33]. One of the serious problems in producing seed of borage is unlimited process of flower and seed falling. Seeds become mature about 3 weeks after pollination. Plant continues to flowering while seeds are falling. Average rate of seeding is estimated about 400 kg per hectare of which 320 kg is fallen and 80 kg can be harvested^[30].

2.4. Chemical compounds

2.4.1. Stems, leaves, and flowers

Many researchers have reported about the fatty acids available in leaves or the whole plant of borage, but there are few information about changes in fatty acids during growth period. A research evaluates the quality and the amount of fatty acids available in borage in different growth stages and reported as follows^[4].

The amount of dry matter in all considered growth stages was very low. Chemical compound was closely related

to the growth stages of plant and the amount of fiber was increasingly raised. The amount of raw protein decreased and the amount of lignin showed age-related increase. Indigestibility of the organic substance decreased in the beginning of the seed formation stage. This decrease was attributed to interactions of some factors including significant increase in fibers parts, relative increase in lignin during growth stages and changes in the ratio of plant tissues components. The amount of total energy was almost constant in first three stages and then increased a little. Since nutritional value during growth period was constant optimum harvest stage of the borage is in the beginning of seed formation stage when performance of dry matter is minimum. The profile of the fatty acids changes upon growth stages. α -Linolenic acid (ALA) and stearidonic acid (SDA) are the main compounds in germination stage which then decreased later. In the beginning of seed formation stage LA is in highest level and the amounts of GLA and acid oleic increase.

The leaves of borage contains following compounds: a few amount of pyrrolizidine alkaloids, licosamin, intermedin, sopinin, sopindian, yezan, colin; fatty acids including ALA (55%) and GLA (more than 4%); silicic acid (1.5%–22.0%); potassium, calcium, nitrate potassium (3%), acetic, lactic and malic acid; δ -bornesitol, cianozhens; fresh leaves also contain mucilage hydrolysable to glucose, galactose, arabinose and alantoein up to 30%; leaves of borage in seeding stage contain 2.5–5.0 mg GLA and 5.7–9.0 mg SDA[34,35]. The most amount of the gamma-linolenic fatty acids are seen in May or June and the most amount of that in upper leaves of the stem in August or September[36].

The amount of gum and mucilage available in leave and stem is 3.8% and in inflorescence is 5.4%. The amounts of potassium and calcium are reported 5.3% and 6.2% respectively[11,37,38]. Compared to inflorescence, less amounts of potassium, gum and mucilage are present in stem and leave but more calcium is in stem and leave. Inflorescence of borage contains mucilage, tannin, calcium, potassium and ash insoluble in acid and alkaloid but has not saponins, flavonoids and cyanogenic glycosides[1,19,20,38]. The flowers of borage and generally all parts of the plant contain 30% mucilage. Green parts of the plant contain nitrate potassium, resin, malate and a little amount of essence, manganese, phosphoric acid and allantoin[39–41].

SDA is a precursor for prostaglandin synthesis which is found a little in oil of the borage seed while SDA is second frequent fatty acid in leaves of borage[11,42]. Since animals have very low ability to synthesize this kind of necessary fatty acids, they must be included in daily diet. This vital compounds bearing therapeutic value could increase animals health and quality of life[4]. Linolenic acid and palmetic acid are collected from flowers and high levels of ALA is in mature leaves[42].

2.4.2. Seed

Boraginaceae family is one of the most known resources of GLA. In a chemotaxonomic study on 45 plant biomasses from Boraginaceae family it was determined that all biomasses contain GLA and the lowest amount (7%) was related to *Cerithe major* L. species and the highest amount related to borage species (28%). This fatty acid is available in plant in a few amounts but is very important due to its nutritional and medicinal value[43]. SDA is other fatty acid which is found in plants in a little amount but it is found in Boraginaceae family in amount of 2%[7]. Several studies have been conducted on combination of fatty acid available in seed oil of planted and wild species of Boraginaceae. The amount of linoleic acid, ALA, GLA, SDA and erucic acid are of special importance in chemotaxonomic inside this family. Tocopherols are also natural effective antioxidants and borage species have high amount of δ -tocopherols[44,45].

Phenolic compounds exist in oil seeds and various studies have proved their antioxidant properties. Borage is important due to high amount of GLA available in its seed oil. In a comprehensive research, antioxidants properties of borage extracts have been reported[46,47]. These excellent antioxidants properties of borage are attributed to phenolic compounds. It has been determined that rosmarinic acid, synergic acid and synaptic acid are main phenolic compounds available in extract of borage seed. Rosmarinic acid is the main component of rosemary extract which is used extensively in food industries. On the other hand synergic acid and synaptic acid are included in phenol and main antioxidants of rapeseed and canola[39,48,49].

There is potential for borage antioxidants to be used in food formulations and in skin health products as compounds which absorb UV. It has been suggested that linoleic acid and palmitic acid are dominant fatty acids available in mature seeds of borage[42]. Borage oil due to high amount of GLA is investigated by food and pharmaceutical research groups[50]. Oils containing GLA is used to treat some diseases resulted from lack of GLA in human[51].

2.5. Pharmaceutical applications

Raw leaf obtained from borage is used as anticonvulsant, bronchodilator, vasodilator. It also has cardio-depression property.

Today GLA and SDA supplements and oils containing these fatty acids are used in diet to meet the shortage of necessary fatty acids and prostaglandin. They also are used in treating thrombosis, inflammation and cancer[51,52].

Atopic dermatitis is an inherited and regressive disease which is seen in 5%–10% of children and now local corticosteroid is often used to remove inflammatory and itchy rashes seen in patients. Results of recent researches have shown that patients affected by this disease due to lack

necessary fatty acids. Borage is one of the rich resources of these acids and seems to be beneficial to these patients. Borage also has effect on the treatment of obsessive-compulsive disorder. It has been determined that the extract of this plant is effective on stress models in mouse. Studies have shown that patients affected to psoriasis due to lack free fatty acids and if this lack is removed symptoms will be decreased and even recovered. Borage plant is one of the rich resources of GLA which effect on recovery of inflammatory chronic diseases is approved. Borage seed oil has been affective on recovery of *Psoriasis vulgaris* rashes[53–55].

Researches about borage seed oil analysis show that existence of alkaloids induced side effects is possible. Borage seed oil is also used for chronic skin inflammatory disease in order to prevent manifestation of these effects. Skin itch and stimulation problems are also ameliorated by this plant extract[49,56]. Several plants in Boraginaceae family, specially Borage and its Iranian variety (*Echium amoenum*), have been used in Iranian traditional medicine as tranquillizer from ancient times. Phytochemical studies have shown presence of flavonoids in this plant and they can produce benzodiazepine like effects by attaching to benzodiazepine receptors. Methanol extract of *Echium amoenum* has also shown anticonvulsant effects in mouse. The main effective substances in this plant are pyrrolizidine alkaloids, flavonoides, rosmarinic acid, anthocyanins, saponins, unsaturated terpenoides and sterol. Likely anticonvulsant effects of this plant are performed by flavonoids, rosmarinic acid and some of the above substances[57]. Of course proof of this subject requires special researches on these substances.

Borage plant causes increase in urine excretion, decrease in blood pressure and kidney function benefits[38,56].

2.6. Effects related to GLA

GLA is one of the compounds available in borage and some other plants seed oil which is extensively used in food supplements and to treat different diseases. Unsaturated fatty acids are very important in animals cells since they are affected in maintaining structure and function of cell membrane, adjusting synthesis and transfer of cholesterol and in avoiding water loss from skin and precursor of eicosanoids like prostaglandins and leucotrienes. In animals these fatty acids are synthesized from necessary fatty acid linolenic acid and first stage of this process is desaturation of GLA by Δ -Desaturase[43]. Synchronous decrease in activity of this enzyme and advancement of age, stress, eczema, diabetes, and some infections or increase in GLA catabolism simultaneously due to oxidation or fast cell division leads to GLA lack. Clinical experiments have shown that consumption of food supplements containing GLA could be useful in the treatment of some diseases such as local eczema, mastalgia, diabetes, virus infections and some kind of cancers. Oils containing GLA are used vastly as health public supplement

and their medicinal use is approved. Generally GLA is used as food supplement and drug prescript to treat diseases like local eczema, heart diseases, cyclical mastalgia, diabetes, arthritis and multiple sclerosis[58,59]. High validity of borage and its increasing demand is related to increase in documents about fatty acids quality and also their amount in human diet regarding health and effect of improving atherosclerosis. Polyunsaturated fatty acids are not synthesized by human body and must be supplied by special diets. They are the most important precursor for active physiological compounds like prostaglandin, thromboxanes and leucotrienes[60]. Human body skin cannot biosynthesize GLA from linolenic acid or arachidonic acid precursor. So daily consumption of borage seed oil which is rich in GLA significantly improves skin condition. After using this oil skin dryness and itch are decreased[61].

2.7. Antioxidant effects

Fat oxidation is one of the main reasons of decrease in the quality of fatty foods. This process affect on color, flavor, tissue and nutritional value of foods[62]. Free radicals such as superoxide, hydroxyl, hydroperoxyl and nitric oxide radicals can cause fat oxidation[63]. Using synthetic antioxidants in foods could delay oxidation but using them in food products is subject to limitation regarding rules since these compounds have anti-health potential. This subject causes us to prefer natural antioxidants instead of them. Medicinal plants with natural antioxidants have been shown to be beneficial in a variety of complications such as cancer[64–66], burn[67,68], diabetes[69–71], hyperlipidemia[72–74], and amnesia[75,76]. These compounds are able to prevent or cure the side effects of other compounds[71,77–80].

Many natural antioxidants already have been extracted from different kinds of plant materials such as oilseeds, vegetables, leaves, roots, spices, cereal and plants leaves[81]. Among natural antioxidants, phenolic antioxidants are extensively available in plants[66,82–84]. Borage oil is rich in unsaturated fatty acids like GLA which is high resistance to oxidation. This resistance is resulted from existence of tocopherols and several phenol compounds in tissues containing oil. When oil is extracted antioxidants such as tocopherols are extracted with oil which are main factors in protecting the oil. Borage flour contains large amounts of phenol compounds after extracting oil. These antioxidants can be concentrated as raw extracts or be used as phenol compounds in unsaturated oils like seed oils[46,47]. Borage flour and its extracts have concentration-related antioxidant properties. Products containing high amount of antioxidant can be obtained from borage flour under optimum condition. Maximum antioxidant activity of extract is resulted if extraction is performed with 52% ethanol in 74 °C for 60 min. The ability of this extract to delay fat oxidation is attributed to the phenol compounds to eliminate reactive species of oxygen. Borage extract may be added to oils and meat products instead of antioxidants to delay fats oxidation. But, low amount of the hydrophobic phenols may lead to weak

antioxidant in oil emulsion systems in water.

Transition metal ions like iron, magnesium, manganese are also found frequently in living beings and foods with plant and animal origin. These metals interfere directly or indirectly in the beginning of fat oxidation. It has been determined that chelated form of metal ions to fat peroxidation is less available. Since raw extract of borage and its components have chelating property of metals in watery experimental environment, this extract could be considered as a good chelating factor for food and other products^[49,85–87].

Regarding ability of borage extract to scavenge reactive oxygen species and DPPH radical, it could be used as relative drug to treat diseases related to free radicals which might hurt tissues^[88]. Borage meal imposes an antioxidant activity which is dependent on concentration in meat model system. Antioxidant compounds are concentrated in a meal in the best condition of extraction which is predicted by response surface methodology that is 52% ethanol at 74 °C for 60 min^[85].

3. Conclusion

Borage is cultivated for medicinal and culinary uses, even though it is commercially cultivated for borage seed oil. Borage seed oil is rich in GLA which is used as dietary or food supplement. Other than seed oil it contains lots of fatty acids such as linoleic acid, oleic acid, palmitic acid, stearic acid, eicosenoic acid and erucic acid. It is used for the treatment of various diseases such as multiple sclerosis, diabetes, heart diseases, arthritis and eczema. For these reasons its cultivation has been carried out recently.

Conflict of interest statement

We declare that we have no conflict of interest.

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